

independently, hydrogen, trifluoromethyl or methyl, or one of R_{13} and R_{14} is cyano and the other is hydrogen or methyl, or $-C(R_{13}R_{14})$ is a cyclopropyl group, or Z is nitrogen or CH and forms a five or six membered heterocyclic ring fused with R_5 , which ring optionally includes two or three further hetero members selected independently from oxygen, nitrogen, NR_{12} , and $S(O)_m$, and optionally includes from one to three double bonds, and is optionally substituted with halo, C_1 - C_4 alkyl, $-O(C_1$ - C_4 alkyl), NH_2 , $NHCH_3$, $N(CH_3)_2$, CF_3 , or OCF_3 , with the proviso that said ring does not include any $-S-S-$, $-S-O-$, $-N-S-$, or $-O-O-$ bonds, and does not include more than two oxygen or $S(O)_m$ heterologous members;

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R_1 is $C(O)H$, $C(O)(C_1$ - C_6 alkyl), $C(O)(C_1$ - C_6 alkylene)(C_3 - C_8 cycloalkyl), $C(O)(C_3$ - C_8 cycloalkylene)(C_3 - C_8 cycloalkyl), $C(O)(C_1$ - C_6 alkylene)(C_4 - C_8 heterocycloalkyl), $-C(O)(C_3$ - C_8 cycloalkylene)(C_4 - C_8 heterocycloalkyl), C_1 - C_6 alkyl, C_3 - C_8 cycloalkyl, C_4 - C_8 heterocycloalkyl, $-(C_1$ - C_6 alkylene)(C_3 - C_8 cycloalkyl), $-(C_3$ - C_8 cycloalkylene)(C_3 - C_8 cycloalkyl), $-(C_1$ - C_6 alkylene)(C_4 - C_8 heterocycloalkyl), $-(C_3$ - C_8 cycloalkylene)(C_4 - C_8 heterocycloalkyl), or $-O$ -aryl, or $-O-(C_1$ - C_6 alkylene)-aryl; wherein said aryl, C_4 - C_8 heterocycloalkyl, C_1 - C_6 alkyl, C_3 - C_8 cycloalkyl, C_3 - C_8 cycloalkylene, and C_1 - C_6 alkylene groups may each independently be optionally substituted with from one to six fluoro and may each independently be optionally substituted with one or two substituents R_8 independently selected from the group consisting of C_1 - C_4 alkyl, $-C_3$ - C_8 cycloalkyl, hydroxy, chloro, bromo, iodo, CF_3 , $-O-(C_1$ - C_6 alkyl), $-O-(C_3$ - C_5 cycloalkyl), $-O-CO-(C_1$ - C_4 alkyl), $-O-CO-NH(C_1$ - C_4 alkyl), $-O-CO-N(R_{24})(R_{25})$, $-N(R_{24})(R_{25})$, $-S(C_1$ - C_4 alkyl), $-S(C_3$ - C_5 cycloalkyl), $-N(C_1$ - C_4 alkyl) $CO(C_1$ - C_4 alkyl), $-NHCO(C_1$ - C_4 alkyl), $-COO(C_1$ - C_4 alkyl), $-CONH(C_1$ - C_4 alkyl), $-CON(C_1$ - C_4 alkyl) $(C_1$ - C_2 alkyl), CN , NO_2 , $-OSO_2(C_1$ - C_4 alkyl), $S^+(C_1$ - C_6 alkyl) $(C_1$ - C_2 alkyl) I^- , $-SO(C_1$ - C_4 alkyl) and $-SO_2(C_1$ - C_4 alkyl); and wherein the C_1 - C_6 alkyl, C_1 - C_6 alkylene, C_5 - C_8 cycloalkyl, C_5 - C_8 cycloalkylene, and C_5 - C_8 heterocycloalkyl moieties of R_1 may optionally independently include from one to three double or triple bonds; and wherein the C_1 - C_4 alkyl moieties and C_1 - C_6 alkyl moieties of R_8 can optionally independently be substituted with hydroxy, amino, C_1 - C_4 alkyl, aryl, $-CH_2$ -aryl, C_3 - C_5 cycloalkyl, or $-O-(C_1$ - C_4 alkyl), and can optionally independently be substituted with from one to six fluoro, and can optionally include one or two double or triple bonds; and wherein each heterocycloalkyl group of R_1 includes from one to three heteromieties selected from oxygen, $S(O)_m$, nitrogen, and NR_{12} ;

R_2 is hydrogen, C_1 - C_{12} alkyl, C_3 - C_8 cycloalkyl, C_4 - C_8 heterocycloalkyl, $-(C_1$ - C_6 alkylene)(C_3 - C_8 cycloalkyl), $-(C_3$ - C_8 cycloalkylene)(C_3 - C_8 cycloalkyl), $-(C_1$ - C_6 alkylene)(C_4 - C_8 heterocycloalkyl), $-(C_3$ - C_8 cycloalkylene)(C_4 - C_8 heterocycloalkyl), aryl, $-(C_1$ - C_6 alkylene)aryl, or $-(C_3$ - C_8 cycloalkylene)(aryl); wherein each of the foregoing R_2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, and C_1 - C_6 alkyl, wherein one of said one to three substituents can further be selected from bromo, iodo, C_1 - C_6 alkoxy, $-OH$, $-O-CO-(C_1$ - C_6 alkyl), $-O-CO-N(C_1$ - C_4 alkyl) $(C_1$ - C_2 alkyl), $-S(C_1$ - C_6 alkyl), $-S(O)(C_1$ - C_6 alkyl), $-S(O)_2(C_1$ - C_6 alkyl), $S^+(C_1$ - C_6 alkyl) $(C_1$ - C_2 alkyl) I^- , CN , and NO_2 ; and wherein the C_1 - C_{12} alkyl, $-(C_1$ - C_6 alkylene), $-(C_5$ - C_8 cycloalkyl), $-(C_5$ - C_8 cycloalkylene), and $-(C_5$ - C_8 heterocycloalkyl) moieties of R_2

may optionally independently include from one to three double or triple bonds; and wherein each heterocycloalkyl group of R_2 includes from one to three heteromoieties selected from oxygen, $S(O)_m$, nitrogen, and NR_{12} ;

or when R_1 and R_2 are as in $-NHCHR_1R_2$, $-OCHR_1R_2$, $-SCHR_1R_2$, $-CHR_1R_2$ or $-NR_1R_2$, R_1 and R_2 of B may form a saturated 5- to 8-membered ring which may optionally include one or two double bonds and in which one or two of the ring carbons may optionally be replaced by an oxygen, $S(O)_m$, nitrogen or NR_{12} ; and which ring can optionally be substituted with from 1 to 3 substituents selected from the group consisting of hydroxy, C_1 - C_4 alkyl, fluoro, chloro, bromo, iodo, CF_3 , $-O-(C_1-C_4$ alkyl), $-O-CO-(C_1-C_4$ alkyl), $-O-CO-NH(C_1-C_4$ alkyl), $-O-CO-N(C_1-C_4$ alkyl)(C_1-C_2 alkyl), $-NH(C_1-C_4$ alkyl), $-N(C_1-C_2$ alkyl)(C_1-C_4 alkyl), $-S(C_1-C_4$ alkyl), $-N(C_1-C_4$ alkyl) $CO(C_1-C_4$ alkyl), $-NHCO(C_1-C_4$ alkyl), $-COO(C_1-C_4$ alkyl), $-CONH(C_1-C_4$ alkyl), $-CON(C_1-C_4$ alkyl)(C_1-C_2 alkyl), CN , NO_2 , $-OSO_2(C_1-C_4$ alkyl), $-SO(C_1-C_4$ alkyl), and $-SO_2(C_1-C_4$ alkyl), wherein one of said one to three substituents can further be selected from phenyl;

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R_3 is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF_3 , NH_2 , $NH(C_1-C_2$ alkyl), $N(CH_3)_2$, $-NHCOCF_3$, $-NHCH_2CF_3$, $S(O)_m(C_1-C_4$ alkyl), $CONH_2$, $-CONHCH_3$, $CON(CH_3)_2$, $-CF_3$, or CH_2OCH_3 ;

R_4 is hydrogen, C_1 - C_4 alkyl, C_3 - C_5 cycloalkyl, $-(C_1-C_4$ alkylene)(C_3 - C_5 cycloalkyl), $-(C_3-C_5$ cycloalkylene)(C_3 - C_5 cycloalkyl), cyano, fluoro, chloro, bromo, iodo, $-OR_{24}$, C_1 - C_6 alkoxy, $-O-(C_3-C_5$ cycloalkyl), $-O-(C_1-C_4$ alkylene)(C_3 - C_5 cycloalkyl), $-O-(C_3-C_5$ cycloalkylene)(C_3 - C_5 cycloalkyl), $-CH_2SC(S)O(C_1-C_4$ alkyl), $-CH_2OCF_3$, CF_3 , amino, nitro, $-NR_{24}R_{25}$, $-(C_1-C_4$ alkylene)- OR_{24} , $-(C_1-C_4$ alkylene)Cl, $-(C_1-C_4$ alkylene) $NR_{24}R_{25}$, $-NHCOR_{24}$, $-NHCONR_{24}R_{25}$, $-C=NOR_{24}$, $-NHNR_{24}R_{25}$, $-S(O)_mR_{24}$, $-C(O)R_{24}$, $-OC(O)R_{24}$, $-C(O)CN$, $-C(O)NR_{24}R_{25}$, $-C(O)NHNR_{24}R_{25}$, and $-COOR_{24}$, wherein the alkyl and alkylene groups of R_4 may optionally independently include one or two double or triple bonds and may optionally independently be substituted with one or two substituents R_{10} independently selected from hydroxy, amino, $-NHCOCCH_3$, $-NHCOCH_2Cl$, $-NH(C_1-C_2$ alkyl), $-N(C_1-C_2$ alkyl)(C_1-C_2 alkyl), $-COO(C_1-C_4$ alkyl), $-COOH$, $-CO(C_1-C_4$ alkyl), C_1 - C_6 alkoxy, C_1 - C_3 thioalkyl, cyano and nitro, and with one to four substituents independently selected from fluoro and chloro;

R_5 is aryl or heteroaryl and is substituted with from one to four substituents R_{27} independently selected from halo, C_1 - C_{10} alkyl, $-(C_1-C_4$ alkylene)(C_3 - C_8 cycloalkyl), $-(C_1-C_4$ alkylene)(C_4 - C_8 heterocycloalkyl), $-(C_3-C_8$ cycloalkyl), $-(C_4-C_8$ heterocycloalkyl), $-(C_3-C_8$ cycloalkylene)(C_3 - C_8 cycloalkyl), $-(C_3-C_8$ cycloalkylene)(C_4 - C_8 heterocycloalkyl), C_1 - C_4 haloalkyl, C_1 - C_4 haloalkoxy, nitro, cyano, $-NR_{24}R_{25}$, $-NR_{24}COR_{25}$, $-NR_{24}CO_2R_{26}$, $-COR_{24}$, $-OR_{25}$, $-CONR_{24}R_{25}$, $-CO(NOR_{22})R_{23}$, $-CO_2R_{26}$, $-C=N(OR_{22})R_{23}$, and $-S(O)_mR_{23}$; wherein said C_1 - C_{10} alkyl, C_3 - C_8 cycloalkyl, $(C_1-C_4$ alkylene), $(C_3-C_8$ cycloalkyl), $(C_3-C_8$ cycloalkylene), and $(C_4-C_8$ heterocycloalkyl) groups can be optionally substituted with from one to three substituents independently selected from C_1 - C_4 alkyl, C_3 - C_8 cycloalkyl, $(C_1-C_4$ alkylene)(C_3 - C_8 cycloalkyl), $-(C_3-C_8$ cycloalkylene)(C_3 - C_8 cycloalkyl), C_1 - C_4 haloalkyl, hydroxy, C_1 - C_6 alkoxy, nitro, halo, cyano, $-NR_{24}R_{25}$, $-NR_{24}COR_{25}$,

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$\text{NR}_{24}\text{CO}_2\text{R}_{26}$, $-\text{COR}_{24}$, $-\text{OR}_{25}$, $-\text{CONR}_{24}\text{R}_{25}$, CO_2R_{26} , $-\text{CO}(\text{NOR}_{22})\text{R}_{25}$, and $-\text{S}(\text{O})_m\text{R}_{23}$; and wherein two adjacent substituents of the R_5 group can optionally form a 5-7 membered ring, saturated or unsaturated, fused to R^5 , which ring optionally can include one, two, or three heterologous members independently selected from O, $\text{S}(\text{O})_m$, and N, but not any $-\text{S}-\text{S}-$, $-\text{O}-\text{O}-$, $-\text{S}-\text{O}-$, or $-\text{N}-\text{S}-$ bonds, and which ring is optionally substituted with $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_3\text{-C}_8$ cycloalkyl, $-(\text{C}_1\text{-C}_4$ alkylene) $(\text{C}_3\text{-C}_8$ cycloalkyl), $-(\text{C}_3\text{-C}_8$ cycloalkylene) $(\text{C}_3\text{-C}_8$ cycloalkyl), $\text{C}_1\text{-C}_4$ haloalkyl, nitro, halo, cyano $-\text{NR}_{24}\text{R}_{25}$, $\text{NR}_{24}\text{COR}_{25}$, $\text{NR}_{24}\text{CO}_2\text{R}_{26}$, $-\text{COR}_{24}$, $-\text{OR}_{25}$, $-\text{CONR}_{24}\text{R}_{25}$, CO_2R_{26} , $-\text{CO}(\text{NOR}_{26})\text{R}_{25}$, or $-\text{S}(\text{O})_m\text{R}_{23}$; wherein one of said one to four optional substituents R_{27} can further be selected from $-\text{SO}_2\text{NH}(\text{C}_1\text{-C}_4$ alkyl), $-\text{SO}_2\text{NH}(\text{C}_1\text{-C}_4$ alkylene) $(\text{C}_3\text{-C}_8$ cycloalkyl), $-\text{SO}_2\text{NH}(\text{C}_3\text{-C}_8$ cycloalkyl), $-\text{SO}_2\text{NH}(\text{C}_3\text{-C}_8$ cycloalkylene) $(\text{C}_3\text{-C}_8$ cycloalkyl), $-\text{SO}_2\text{N}(\text{C}_1\text{-C}_4$ alkyl) $(\text{C}_1\text{-C}_2$ alkyl), $-\text{SO}_2\text{NH}_2$, $-\text{NHSO}_2(\text{C}_1\text{-C}_4$ alkyl), $-\text{NHSO}_2(\text{C}_3\text{-C}_8$ cycloalkyl), $-\text{NHSO}_2(\text{C}_1\text{-C}_4$ alkylene) $(\text{C}_3\text{-C}_8$ cycloalkyl), and $-\text{NHSO}_2(\text{C}_3\text{-C}_8$ cycloalkylene) $(\text{C}_3\text{-C}_8$ cycloalkyl); and wherein the alkyl, and alkylene groups of R_5 may independently optionally include one double or triple bond;

R_6 is hydrogen, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_3\text{-C}_8$ cycloalkyl, $-(\text{C}_1\text{-C}_6$ alkylene) $(\text{C}_3\text{-C}_8$ cycloalkyl), or $-(\text{C}_3\text{-C}_8$ cycloalkylene) $(\text{C}_3\text{-C}_8$ cycloalkyl), wherein said alkyl and cycloalkyl may optionally be substituted with one hydroxy, methoxy, ethoxy or fluoro group;

R_7 is hydrogen, methyl, fluoro, chloro, bromo, iodo, cyano, hydroxy, $-\text{O}(\text{C}_1\text{-C}_2$ alkyl), $-\text{O}(\text{cyclopropyl})$, $-\text{COO}(\text{C}_1\text{-C}_2$ alkyl), $-\text{COO}(\text{C}_3\text{-C}_8$ cycloalkyl), $-\text{OCF}_3$, CF_3 , $-\text{CH}_2\text{OH}$, or CH_2OCH_3 ;

R_{11} is hydrogen, hydroxy, fluoro, ethoxy, or methoxy;

R_{12} is hydrogen or $\text{C}_1\text{-C}_4$ alkyl;

R_{22} is independently at each occurrence selected from hydrogen, $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_1\text{-C}_4$ haloalkyl, $\text{C}_3\text{-C}_6$ alkenyl, $\text{C}_3\text{-C}_6$ alkynyl, $\text{C}_3\text{-C}_8$ cycloalkyl, $(\text{C}_3\text{-C}_8$ cycloalkylene) $(\text{C}_3\text{-C}_8$ cycloalkyl), and $(\text{C}_1\text{-C}_4$ alkylene) $(\text{C}_3\text{-C}_8$ cycloalkyl);

R_{23} is independently at each occurrence selected from $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_1\text{-C}_4$ haloalkyl, $\text{C}_2\text{-C}_8$ alkoxyalkyl, $\text{C}_3\text{-C}_8$ cycloalkyl, $-(\text{C}_1\text{-C}_4$ alkylene) $(\text{C}_3\text{-C}_8$ cycloalkyl), $-(\text{C}_3\text{-C}_8$ cycloalkylene) $(\text{C}_3\text{-C}_8$ cycloalkyl), aryl, $-(\text{C}_1\text{-C}_4$ alkylene)aryl, piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine, and thiomorpholine;

R_{24} and R_{25} are independently at each occurrence selected from hydrogen, $-\text{C}_1\text{-C}_4$ alkyl, $\text{C}_1\text{-C}_4$ haloalkyl, especially CF_3 , $-\text{CHF}_2$, CF_2CF_3 , or CH_2CF_3 , $-(\text{C}_1\text{-C}_4$ alkylene) OH , $-(\text{C}_1\text{-C}_4$ alkylene) $-\text{O}(\text{C}_1\text{-C}_4$ alkyl), $-(\text{C}_1\text{-C}_4$ alkylene) $-\text{O}-(\text{C}_3\text{-C}_5$ cycloalkyl), $\text{C}_3\text{-C}_8$ cycloalkyl, $-(\text{C}_1\text{-C}_4$ alkylene) $(\text{C}_3\text{-C}_8$ cycloalkyl), $-(\text{C}_3\text{-C}_8$ cycloalkylene) $(\text{C}_3\text{-C}_8$ cycloalkyl), $-\text{C}_4\text{-C}_8$ heterocycloalkyl, $-(\text{C}_1\text{-C}_4$ alkylene) $(\text{C}_4\text{-C}_8$ heterocycloalkyl), $-(\text{C}_3\text{-C}_8$ cycloalkylene) $(\text{C}_4\text{-C}_8$ heterocycloalkyl), aryl, and $-(\text{C}_1\text{-C}_4$ alkylene)(aryl), wherein the $-\text{C}_4\text{-C}_8$ heterocycloalkyl groups can each independently optionally be substituted with aryl, CH_2 -aryl, or $\text{C}_1\text{-C}_4$ alkyl, and can optionally include one or two double or triple bonds; or, when R_{24} and R_{25} are as $\text{NR}_{24}\text{R}_{25}$, $-\text{C}(\text{O})\text{NR}_{24}\text{R}_{25}$, $-(\text{C}_1\text{-C}_4$ alkylene) $\text{NR}_{24}\text{R}_{25}$, or $-\text{NHCONR}_{24}\text{R}_{25}$, then $\text{NR}_{24}\text{R}_{25}$ may further optionally form a 4 to 8 membered heterocyclic ring optionally including one or two further hetero members independently selected from $\text{S}(\text{O})_m$, oxygen,

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~~nitrogen, and NR₁₂, and optionally including from one to three double bonds;~~

~~R₂₆ is independently at each occurrence selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₃-C₈ cycloalkyl, -(C₁-C₄ alkylene)(C₃-C₈ cycloalkyl), -(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), aryl, and -(C₁-C₄ alkylene)(aryl); and~~

~~wherein each m is independently zero, one, or two,~~

~~with the proviso that heterocycloalkyl groups of the compound of formula I do not include any -S-S-, -S-O-, -N-S-, or -O-O- bonds, and do not include more than two oxygen or S(O)_m heterologous members.~~

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9. (AMENDED) A pharmaceutical composition for the treatment of (a) a disorder or condition the treatment of which can be effected or facilitated by antagonizing CRF, or (b) a disorder or condition selected from inflammatory disorders such as rheumatoid arthritis and osteoarthritis, pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias, including social phobia, agoraphobia, and specific phobias; obsessive-compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception such as fibromyalgia; mood disorders such as depression, including major depression, single episode depression, recurrent depression, child abuse induced depression, mood disorders associated with premenstrual syndrome, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; chronic fatigue syndrome; stress-induced headache; irritable bowel syndrome; spastic colon; post operative ileus; ulcer; diarrhea; stress-induced fever; neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and Huntington's disease; gastrointestinal diseases; hemorrhagic stress; chemical dependencies or addictions, including dependencies or addictions to alcohol, cocaine, heroin, benzodiazapines, or other drugs; drug or alcohol withdrawal symptoms; stress-induced psychotic episodes; euthyroid sick syndrome; syndrome of inappropriate antidiuretic hormone; head trauma; spinal cord trauma; ischemic neuronal damage, including cerebral ischemia, for example cerebral hippocampal ischemia; excitotoxic neuronal damage; epilepsy; stroke; immune dysfunctions including stress induced immune dysfunctions, including porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, confinement dysfunction in chicken, sheering stress in sheep, and human-animal interaction stress in dogs; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multiinfarct dementia; amyotrophic lateral sclerosis; hypertension; tachycardia; congestive heart failure; osteoporosis and premature birth in a mammal or bird, comprising an amount of a compound according to claim 1 that is effective in the treatment of such disorder or condition, and a pharmaceutically acceptable carrier.

10. (AMENDED) A method for the treatment of (a) a disorder or condition the treatment of which can be effected or facilitated by antagonizing CRF, or (b) a disorder or condition selected from inflammatory disorders such as rheumatoid arthritis and osteoarthritis,

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pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias, including social phobia, agoraphobia, and specific phobias; obsessive-compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception such as fibromyalgia; mood disorders such as depression, including major depression, single episode depression, recurrent depression, child abuse induced depression, mood disorders associated with premenstrual syndrome, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; chronic fatigue syndrome; stress-induced headache; irritable bowel syndrome spastic colon; post operative ileus; ulcer; diarrhea; stress-induced fever; neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and Huntington's disease; gastrointestinal diseases; hemorrhagic stress; chemical dependencies or addictions, including dependencies or addictions to alcohol, cocaine, heroin, benzodiazapines, or other drugs; drug or alcohol withdrawal symptoms; stress-induced psychotic episodes; euthyroid sick syndrome; syndrome of inappropriate antidiuretic hormone; head trauma; spinal cord trauma; ischemic neuronal damage, including cerebral ischemia, for example cerebral hippocampal ischemia; excitotoxic neuronal damage; epilepsy; stroke; immune dysfunctions including stress induced immune dysfunctions, including porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, confinement dysfunction in chicken, sheering stress in sheep, and human-animal interaction stress in dogs; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multiinfarct dementia; amyotrophic lateral sclerosis; hypertension; tachycardia; congestive heart failure; osteoporosis and premature birth in a mammal or bird, comprising administering to a subject in need of said treatment an amount of a compound according to claim 1, that is effective in treating such disorder or condition.

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17. A pharmaceutical composition for treating a condition comprising a compound of claim 1 in an amount effective to treat said condition and a pharmaceutically acceptable carrier, wherein said condition is selected from the group consisting of:

- a) abnormal circadian rhythm;
- b) depression, further wherein a second compound for treating depression is administered, said second compound for treating depression having an onset of action that is delayed with respect to that of said compound of claim 1; and
- c) emesis.

REMARKS

Claims 1 - 22 are now pending in the application. Claims 1, 9, 10, and 17 have been amended herein. A clean copy of the amended claims now pending in the application has been provided. A marked up version of the amended claims is appended.

No new matter has been introduced by virtue of the amendments made herein. Accordingly, applicants respectfully request their entry. In view of the amendments made herein

and the remarks below, applicants respectfully request reconsideration and withdrawal of the rejection set forth in the January 29, 2003 office action.

Rejection under 35 USC § 112, second paragraph

The Examiner rejected claims 1-7, and 9-22 under 35 USC § 112, second paragraph for indefiniteness.

a. Reference to deleted formulae II and III in the proviso of claim 1 has been deleted. Applicant submits twice amended claim 1 is patentable under 35 USC § 112, second paragraph and respectfully requests withdrawal of the rejection.

b. Without prejudice and in the interests of facilitating prosecution applicant has amended claims 9 and 10 by deletion of the terms "cancer," "human immunodeficiency virus infections," "infertility," "obesity," "anorexia," "bulimia nervosa," "hypoglycemia," "Crohn's disease" and "SyndromeX". Applicant submits amended claims 9 and 10 are patentable under 35 USC § 112, second paragraph and respectfully requests withdrawal of the rejection.

c. Claims 9 and 17 were deemed by the Examiner as substantial duplicates. Claim 17 was amended by deletion, without prejudice, of the term "CRF antagonist" and insertion of the term "compound of claim 1" in its place. Applicant submits claim 17, as amended, differs substantially from claim 9 in its recital of "A pharmaceutical composition for treating..." the condition of "abnormal circadian rhythm" and "emesis" neither of which are specifically recited by claim 9 and by its recital of a pharmaceutical composition for the treatment of "depression" to be used "wherein a second compound for treating depression is administered ... having an onset of action ... delayed with respect to that of said compound of claim 1..." which is also not recited by claim 9. Applicant submits amended claims 9 and 17 are patentable under 35 USC § 112, second paragraph and respectfully requests withdrawal of the rejection.

d. The Examiner rejected claim 20 due to an alleged lack of antecedent basis because it recites "said second compound" which is not recited in claim 17. Applicant submits the Examiner errs since original and now amended claim 17 recite "b) depression, further wherein a *second compound* for treating depression is administered,..." Applicant submits claim 20 is patentable under 35 USC § 112, second paragraph and respectfully requests withdrawal of the rejection.

e. The Examiner rejected claims 2 – 7, 11-16, 18, 19, 21, and 22 "as being (ultimately) dependent on claim 1, 9 or 10, and carry over their limitations." Applicant submits that in view of the foregoing responses and amendments all of these claims are patentable under 35 USC § 112, second paragraph and respectfully requests withdrawal of the rejection.

Double Patenting

The Examiner rejected claims 1, 6, 7, 9 - 11, and 17 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, and 12 - 15 of US Patent No. 5,962,479. The Examiner also provisionally rejected claims 1, 2, 5 - 7, 9, and 10 under the aforementioned doctrine as unpatentable over claims 45, and 56 - 59 of copending Application No. 08/765, 110. Without prejudice and in the interest of facilitating prosecution applicant has appended a terminal disclaimer thereby overcoming both the actual and the provisional rejection of the above claims. Applicant respectfully requests the Examiner withdraw the rejection of claims 1, 6, 7, 9 - 11, and 17 and the provisional rejection of claims 1, 2, 5 - 7, 9, and 10.

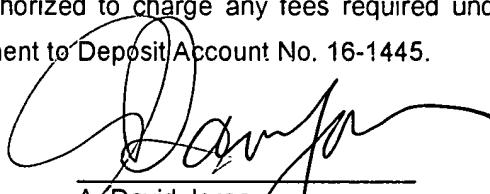
Claim Objections

The Examiner objected to claim 8 as being dependent on a rejected base claim but conceded claim 8 would be allowable if rewritten in independent form. Applicants submit that the base claim, claim 1, is in allowable condition for the reasons given above and respectfully request withdrawal of the objection to claim 8.

In view of the amendments set forth herein and remarks above and the appended terminal disclaimer, the applicant respectfully submits that the pending claims are fully allowable, and solicits the issuance of a notice to such effect. If a telephone interview is deemed to be helpful to expedite the prosecution of the subject application, the Examiner is invited to contact applicant's undersigned attorney at the telephone number provided.

The Commissioner is hereby authorized to charge any fees required under 37 C.F.R. §§1.16 and 1.17 or to credit any overpayment to Deposit Account No. 16-1445.

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